Cost-effectiveness analysis of Pemigatinib for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or rearrangement that have progressed after systemic therapy in Greece.

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Introduction

- Cholangiocarcinoma (CCA) is a highly lethal, epithelial cell malignancy(1).
- CCA is part of a group of biliary tract cancers that accounts approximately for 15% of all primary liver cancers and 3% of all gastrointestinal (GI) tumors(2-5).
- CCAs are most commonly adenocarcinomas and comprise 2 main subtypes: intrahepatic (iCCA), initiating from the biliary tree within the liver, and extrahepatic (eCCA), initiating outside the liver parenchyma(6).
- Currently, there are no licensed, targeted or disease-modifying therapies available in the Greek clinical practice to treat relapsed or refractory advanced CCA with fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement.
- Thus, there is an unmet need for molecularly targeted therapies with an acceptable toxicity profile that achieve disease control, delay worsening of symptoms, maintain HRQoL, delay disease progression, and prolong survival.
- Pemigatinib is a selective, potent, oral inhibitor of FGFR that offers a non-chemotherapy, targeted treatment option to patients with CCA who have FGFR2 translocations.
- Based on its clinical evidence, pemigatinib delivered unprecedented response rates with clinically meaningful and durable responses in CCA patients (7-8).

Objective

To evaluate the cost-effectiveness of pemigatinib compared to oxaliplatin-L-folinic-acid and fluorouracil plus active symptom control (mFOLFOX+ASC) and ASC alone for the treatment of patients with advanced or metastatic CCA with a FGFR2 rearrangement or fusion who have progressed on at least one line of prior systemic therapy in Greece.

Methods

- A partitioned survival model with five health states, was locally adapted from a Greek payer perspective (EOPYY) over a lifetime horizon (Figure 1).
- Efficacy, safety data and utility values were extracted from relevant clinical trials and published studies (7,9-10).
- In the absence of a head-to-head clinical trial, a matching-adjusted indirect comparison of pemigatinib and mFOLFOX+ASC was used (11).
- Cost inputs considered in the model include, drug acquisition & administration costs, monitoring costs, adverse events costs, and end of life costs (Table 1). All costs reflect the year 2022 (€).
- Primary outcomes were patient's life years (LYs), quality-adjusted life years (QALYs), total costs and incremental cost-effectiveness ratios (ICERs).
- Future outcomes that occurred beyond one year were discounted at a 3.5% annual rate which is the standard practice in Greece.
- Probabilistic sensitivity analysis (PSA) and one-way sensitivity analysis (OWSA) were undertaken to deal with uncertainty.

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Figure 1: Model Structure

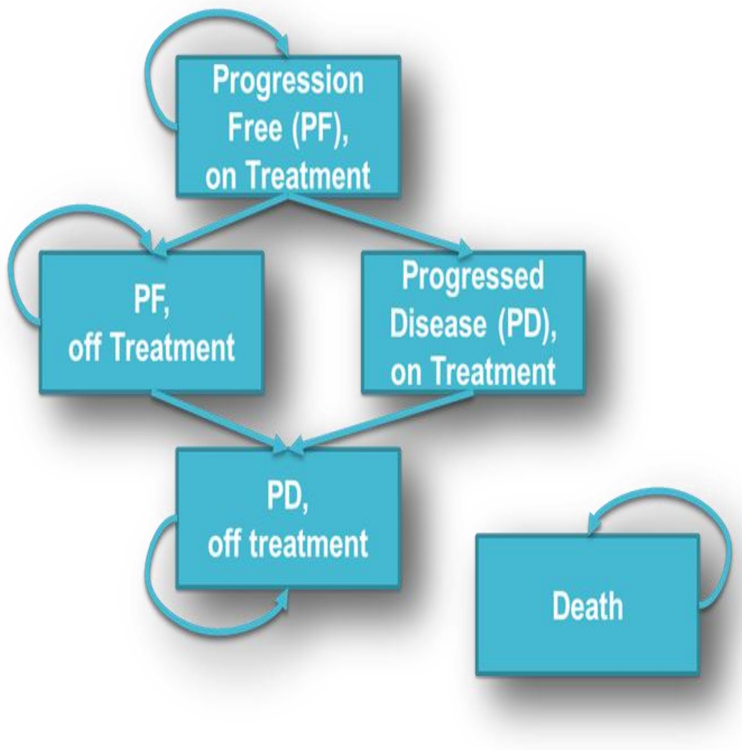


Table 1: The costs inputs considered in the model

Description		Source
Pre-progression costs		
Drug Acquisition Cost per pack (Ex factory price)		
Pemigatinib 13.5 mg	€6,502	Drug bulletin issued by the Greek Ministry of Health (12)
mFOLFOX+ASC		
Oxaliplatin.SOL.IN (5MG/ML BTx1 x 20 ML)	€52.30	
L-folinic acid INJ.SOL 200MG/20ML VIAL BT x1 VIAL	€8.43	
Fluorouracil INJ.SOL 50MG/MLx100 ml	€16.31	
ASC	€0	
Administration Costs	€80	One day clinic, Government Gazette, Ministerial Decision
Annual monitoring cost	€183	ESMO guidelines for biliary cancer &official website of EOPYY (13)
Adverse event		
Abdominal pain	€571	Gourzoulidis et al. 2022(16)
Alanine aminotransferase increased	€145	Gourzoulidis et al. 2022(16)
Anaemia	€487	Gourzoulidis et al. 2019(15)
Anorexia	€277	Gourzoulidis et al. 2018(17)
Arthralgia	€5	Gourzoulidis et al. 2022(16)
Aspartate aminotransferase increased	€149	Gourzoulidis et al. 2022(16)
Billary event	€1,085	DRG code: H08X (14)
Cholangitis	€1,085	DRG code: H08X (14)
Fatigue	€47	Gourzoulidis et al. 2022(16)
Hypophosphataemia	€73	Gourzoulidis et al. 2022 (16)
Infection (lung/urinary/fever/not specified)	€179	Vellopoulou et al. 2021 (18)
Stomatitis	€315	Gourzoulidis et al.2019(15)
Neutropenia	€478	Gourzoulidis et al.2019(15)
Palmar-plantar erythrodysaesthesia syndrome	€75	Gourzoulidis et al.2018(16)
Thromboembolic events	€760	Gourzoulidis et al.2017 (19)
Hyperphosphataemia	€43	Gourzoulidis et al.2019(15)
Post-progression costs		
Annual monitoring cost	€81	ESMO guidelines for biliary cancer &official website of EOPYY (13)
End of life	€713	Gourzoulidis et al.2019(15)

Cost of each adverse event and End of life care cost were directly extracted either from similar published studies that were carried out in Greece or from official sources such as DRG tariffs and cost data were inflated in 2022 values using the corresponding health inflation rates reported by the Greek National Statistical Service.

Results(1/2)

- The total lifetime cost per patient for pemigatinib, mFOLFOX +ASC and ASC alone were estimated to be €85,534, €1,010 and €2,537, respectively (Table 2).
- In terms of health outcomes, comparing pemigatinib with ASC alone, the former was associated with a 1.84 and 1.22 increment in LYs and QALYs respectively. When compared with mFOLFOX +ASC, pemigatinib was associated with increases of 1.78 LYs and 1.19 QALYs, respectively (Table 2).
- The incremental analysis of pemigatinib versus mFOLFOX +ASC resulted in an ICER of €69,928 per QALY gained and €46,626 per LY gained (Table 2).
- Moreover, when pemigatinib was compared to ASC alone, the incremental analysis resulted in an ICER of €69,345 per QALY gained and €45,935 per LY gained (Table 2).

Results (2/2)

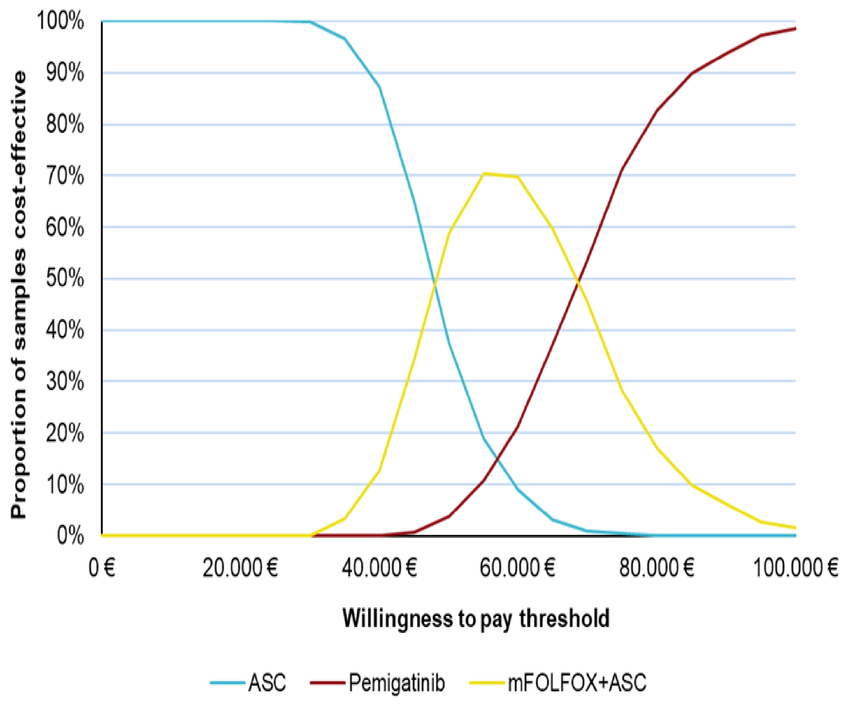
Table 2: Base-case cost-effectiveness results

Parameters	Pemigatinib	ASC	mFOLFOX+ASC
Total cost per patient	€85,534	€1,010	€2,537
LY	2.44	0.60	0.66
QALYs	1.63	0.41	0.44
ICER per LY gained		**€45,935**	**€46,626**
ICER per QALY gained		**€69, 345**	**€69,928**

ASC: Active symptom control, ICER: Incremental cost- effectiveness ratio, LYs: life years, mFOLFOX: oxaliplatin-L-folinic-acid and fluorouracil , QALYs: quality-adjusted life years.

- PSA estimated that at the predefined WTP of €80,000 per QALY gained, treatment with pemigatinib had an 83% probability of being the most cost-effective option compared to all comparators (Figure 2).
- The results of OWSA for the comparison of pemigatinib versus (vs) mFOLFOX +ASC and ASC alone indicated that the most influential parameter on the model were OS hazard ratios. Generally, the model results were stable relative to variation in the model parameters and alternate structural assumptions resulting in similar inferences to be drawn as in the base case analysis

Figure 2: Cost-effectiveness acceptability curve of pemigatinib vs comparators



Conclusion

The results indicate that pemigatinib provides substantial clinical benefit as compared to standard of care at a reasonable cost, and hence, pemigatinib may represent a cost-effective option for adult patients with advanced or metastatic CCA with an FGFR2 rearrangement or fusion who have progressed on at least one line of prior systemic therapy in Greece.

Acknowledgement

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